

## Cholinesterase Testing: Pediatric Clinical Perspective

Catherine Karr MD PhD  
University of Washington  
Region X PEHSU

## Key Issues

Unique clinical diagnostic tool for acute pesticide poisoning

Under recognition of OP poisoning in children  
Kids present differently  
Knowledge gap

Interpretation  
Inter-individual variability

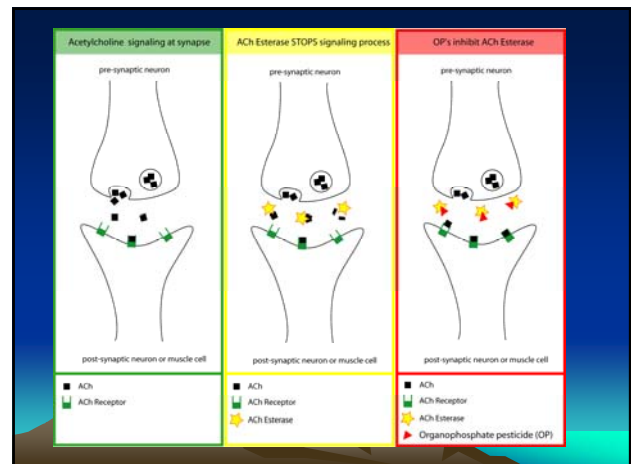
Acute vs chronic toxicity implications

## Cholinesterase Test

Biomarker of biologically active dose

Measures inhibition of cholinesterase enzyme using a blood sample  
Plasma (pseudocholinesterase)  
RBC (acetylcholinesterase)

Surrogate for acetylcholinesterase in the nervous system



## Cholinesterase Inhibitors Toxicity

Effect builds up over time and  
the "Off Switch" gets stuck ON

**M**iosis  
**D**iaphoresis  
**S**alivation  
**L**acrimation  
**U**rination  
**D**efecation  
**G**astroenteric cramping  
**E**mesis



## Clinical Presentation in Children

More likely to have hypotonia & mental status changes  
such as lethargy and coma, seizures

eg. seizure occurrence based on case series:  
adults 2-3%  
children 22-25%

Less likely to have the classic hypersecretion, particularly  
at initial presentation

Often mistaken for viral illness (respiratory infection,  
gastroenteritis, meningitis)

## Under recognition of OP poisoning in children

In one 1980s case series, the diagnosis was incorrect in 16 of 20 cases

In epidemic OP poisoning in midwest, southeast US, missing and delayed diagnosis for months to years

No index of suspicion = no diagnosis

Zwiener. Organophosphate and Carbamate Poisoning in Infants and Children. Pediatrics 1988;81:121-126  
Rubin C. Assessment of human exposure and human health effects after indoor application of methyl parathion in Lorain County, Ohio, 1995-1996. Environ Health Perspect 2002;110(Suppl 6):1047-51.

## Training Gap

Health care providers in NW agricultural setting caring for farmworker families (2005)

Any previous training on pesticides & health? 49%

Child specific info? 22%

Karr et al. Pacific Northwest Health Professionals Survey on Pesticides and Children. Journal of Agromedicine 2006;11:113.

## NW PEHSU Web CME

Organophosphate Pesticides and Child Health: a primer for health care providers

<http://depts.washington.edu/opchild/>

## Diagnostic Testing

If suspect OP exposure

Red blood cell (acetylcholinesterase)  
Plasma (pseudocholinesterase)

Certain OPS may selectively inhibit either plasma or RBC acetylcholinesterase

## Cholinesterase Activity Depression

Occurs w/in few minutes or hours

Effects on plasma enzyme generally persists for several days to a few weeks.

The RBC enzyme activity may take several days to reach its minimum and usually remains depressed longer, sometimes 1-3 months

## Cholinesterase Activity Depression: Interpretation

Great variability in normal general population baseline limits usefulness of reference range

Need to interpret in relation to individual's own baseline – post exposure follow-up with same lab and method

20% increase in plasma OR 15% increase in RBC suggests clinically significant exposure occurred

## Chronic Exposure Toxicity

Cholinesterase testing is limited to diagnosis of clinically significant acute poisoning via the cholinergic pathway

Neurodevelopmental toxicity may occur via alternative mechanisms

Toxicological and epidemiological evidence

## OP Pesticides & Developmental Toxicity: Cholinergic-Independent Mechanism

In vivo evidence (embryonic/neonatal rat models) and in vitro models (neuronal rat cell lines)

Dosage biologically plausible, below amount needed to effectively inhibit acetylcholinesterase

Effects seen throughout brain, including regions with little cholinergic innervation

Cell loss & apoptosis seen immediately after exposure

Neural deficits appear in adolescence & continue into adulthood

Deficits in: brain cell numbers, neurite projections & synaptic communication

## OP Pesticides & Developmental Toxicity: Cholinergic-Independent Mechanism

Several common signaling cascades shown to be effected that are used in many developmental pathways

May help explain widespread & delayed-onset OP effects during development

May explain observations in epidemiological cohort studies

## Implications of Non-Cholinergic Organophosphate Toxicity

Child OP exposure toxicity may result from non-cholinergic endpoints

Clinical markers beyond cholinesterase testing.....

## Beyond cholinesterase testing

Development of clinical application of urinary marker monitoring?

Confirm acute exposures?

Identify concerning chronic exposures?

Influence clinical decision-making?

Preventive guidance

Prognosis

## Agricultural workplace/playground

